UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/944,049 | 08/30/2001 | Thomas J. Schall | 019934-002510US | 8353 |

20350 7590 03/17/2003

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

| EXAMINER | |
|---|---|
| MOSHER, MARY | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1648 | |

DATE MAILED: 03/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/944,049 | SCHALL ET AL |
| **Examiner** | **Art Unit** |
| Mosher | 1648 |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on *1/15/2003, 2/19/2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) *1-71 and 77-110* is/are pending in the application.

4a) Of the above, claim(s) *1-71* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *77-110* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

### *Election/Restriction*

Claims 1-71 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected groups, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 13.

### *Claim Objections*

Claim 80 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 80 requires a carrier comprising Freund's adjuvant or Ribi adjuvant. However, parent claim 78 specifies a pharmaceutically acceptable carrier. Neither of these adjuvants is approved for pharmaceutical use (for example, neither is listed in the 2003 United States Pharmacopeia/National Formulary). Therefore claim 80 goes outside of the scope of parent claim 78.

### *Claim Rejections - 35 USC § 112*

Claims 77-110 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 77-110 are drawn to a vaccine comprising at least a portion of a CMV genome, which is attenuated through inhibition of expression or activity of US28 or a US28 homolog. This is clear enough on its face, but it is not clear that the claims reflect applicant's

intent. Is the intent really to encompass any composition which contains any part of the CMV genome, as long as the composition can't express a functional US28 or US28 homolog, and the composition is capable of generating an immune response in a mammal? Claims of this scope read upon mutant viruses per se (as long as the virus is not combined with any component which makes it impossible to use in vivo), and they also read upon DNA vaccines encoding a single subunit. Is this applicant's intent?

In addition, the claims are confusing in reciting "a vaccine... that can generate an immune response in a mammal." Is the intended scope a composition that can generate an immune response in a mammal, or a vaccine which prevents disease? This affects the scope of the claimed subject matter.

Claims 77-110 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for cytomegaloviruses attenuated through inhibition of expression or activity of US28 and/or a US28 homolog, does not reasonably provide enablement for a vaccine. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. First, the term "vaccine" indicates a composition which induces an immune response protective against disease, and claims 81 and 92 specifically require a human or a rhesus monkey host. The prior art does not provide routine knowledge of any safe and effective vaccines for CMV in either humans or rhesus monkeys, see as evidence the review by Krause et al (Infectious Disease Clinics of North America 13(1):61-81, March 1999). The specification does

not provide any evidence that the claimed compositions are effective in inducing a protective immune response. Second, although prior art such as Beisser et al (Journal of Virology 72(3):2352-2363, 1998 and Journal of Virology 73(9):7218-7230, 1999) teaches that deletion of US28 homologs does attenuate cytomegalovirus, there is no evidence that deletion of one (or even all) of the US28 homologs attenuates the virus sufficiently for safe use in humans or monkeys. This is an issue of particular concern for CMV, considering the ability of CMV to produce a life-long latent infection. Considering the state of the art for CMV vaccines, the unpredictability of safety and efficacy for a CMV vaccine, the limited teachings in the specification, and the absence of any working examples, it is concluded that undue experimentation would be required to enable the full scope of the invention, as claimed.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 77, 78?, 81-83, 84? 86-91 are rejected under 35 U.S.C. 102(b) as being anticipated by Hwang et al (Microbiology and Immunology 43(3):307-310, 1999). Claim 77 is drawn to a vaccine comprising at least a portion of a CMV genome, wherein the genome or portion is attenuated through inhibition of expression or activity of US28 or a US28 homolog. The claim is

drawn to a composition, and does not require any components in the composition other than a portion of a CMV genome with a latent capability to generate an immune response in a mammal. Dependent claims such as 83 indicate that the attenuation can be via deletion of US28 (or homolog). Hwang teaches a composition comprising a portion of a CMV genome, where nearly all of the genome (including the US28, UL33, and UL78 genes) has been deleted. The composition clearly is capable of generating an immune response in a mammal, and reasonably possesses the latent capability to generate an immune response in a human. The reference composition therefore meets each and every limitation of these claims.

Claims 77, 81-83 are rejected under 35 U.S.C. 102(b) as being anticipated by Jones et al (US 5,877,004). Jones teaches a composition containing a human cytomegalovirus with an inactivated US28 gene, see for example column 27, lines 47-61. Although the reference does not teach the intended use recited in the claim preamble, the claim does not specify any components in the composition that distinguish it from the reference composition. Although the reference does not teach a latent capability of the virus to generate an immune response in a mammal or that the virus is attenuated, these are inherent characteristics of the mutated virus. Therefore, the reference composition meets each and every limitation of these claims.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

> such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 92-110 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hwang et al (Microbiology and Immunology 43(3):307-310, 1999) in view of Kropff et al (Journal of General Virology 78:2009-2013, 1997) or Kravitsz et al (Journal of General Virology 78:1999-2007, 1997). Hwang teaches a DNA vaccine comprising DNA encoding HCMV gB (and deleted of all other parts of the HCMV genome, including all the US28 homologs). This differs from the claimed invention, which requires part of the rhCMV genome. However, the secondary references teach an rhCMV homolog of gB. It would have been within the ordinary skill of the art to produce a DNA vaccine to immunize rhesus monkeys, using the rh gB DNA, with reasonable expectation of success. The invention as a whole is therefore prima facie obvious, absent unexpected results.

Beisser et al (Journal of Virology 72(3):2352-2363, 1998 and Journal of Virology 73(9):7218-7230, 1999) are cited as of interest in teaching attenuation of a cytomegalovirus by deletion of UL78 or UL33 homologs.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is (703) 308-2926. The examiner can normally be reached on Monday -Thursday and alternate Fridays from 6:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this Group is now (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

March 14, 2003

MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1800
1600